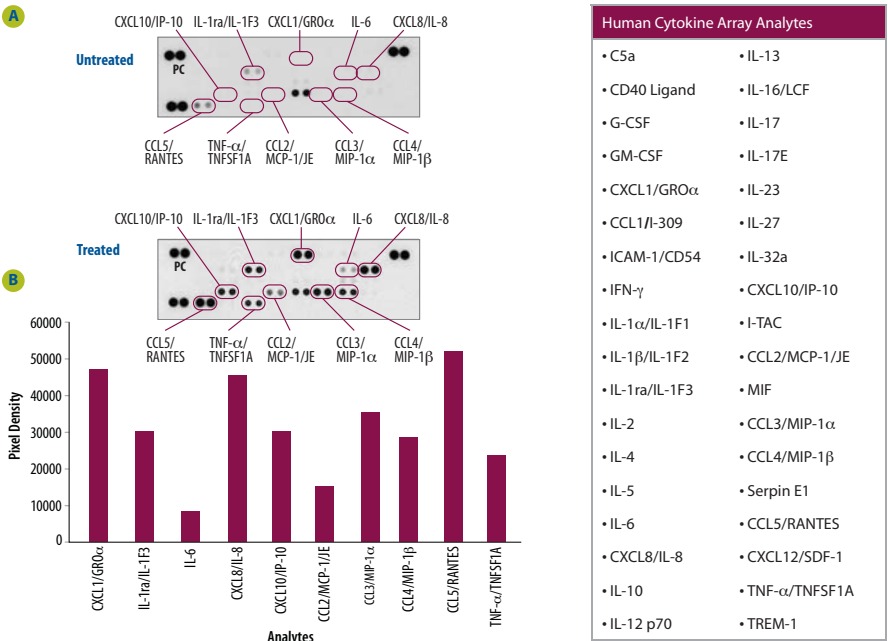
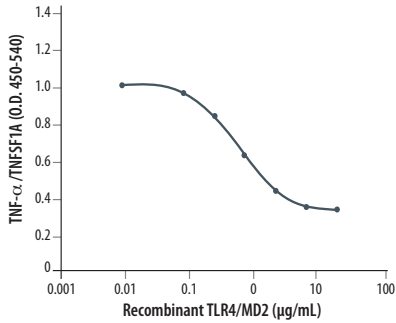


Assessing the Cytokine Response to the TLR Agonist LPS



Detection of Multiple Analytes by Cytokine Array Analysis. **A.** THP-1 cells were untreated or treated with LPS (1 µg/mL) for 16 hours. The conditioned media was assessed for the relative levels of 36 different cytokines using the Proteome Profiler™ Human Cytokine Array Kit (Catalog #ARY005). PC = Positive Control **B.** Histogram profiles for select analytes following LPS treatment were generated by quantifying the mean spot pixel densities from the cytokine array using image analysis software.



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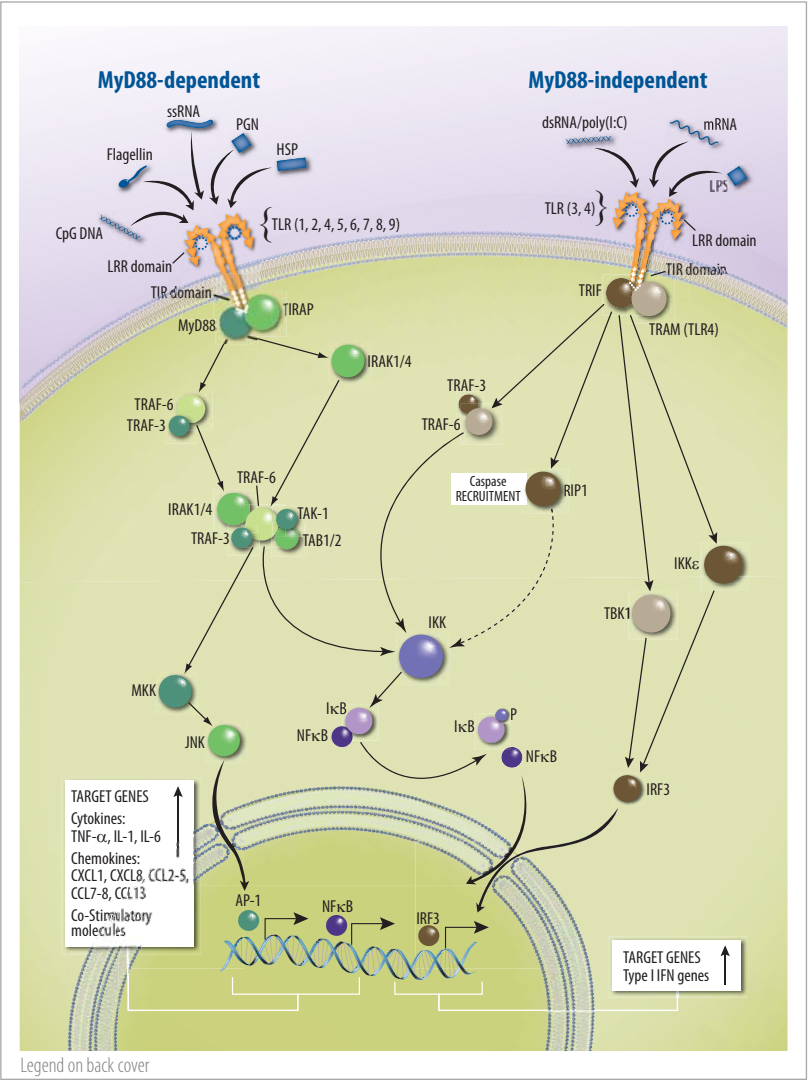


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Toll-like Receptors:
Recognition of Microbial Pathogens
& Induction of the Immune Response

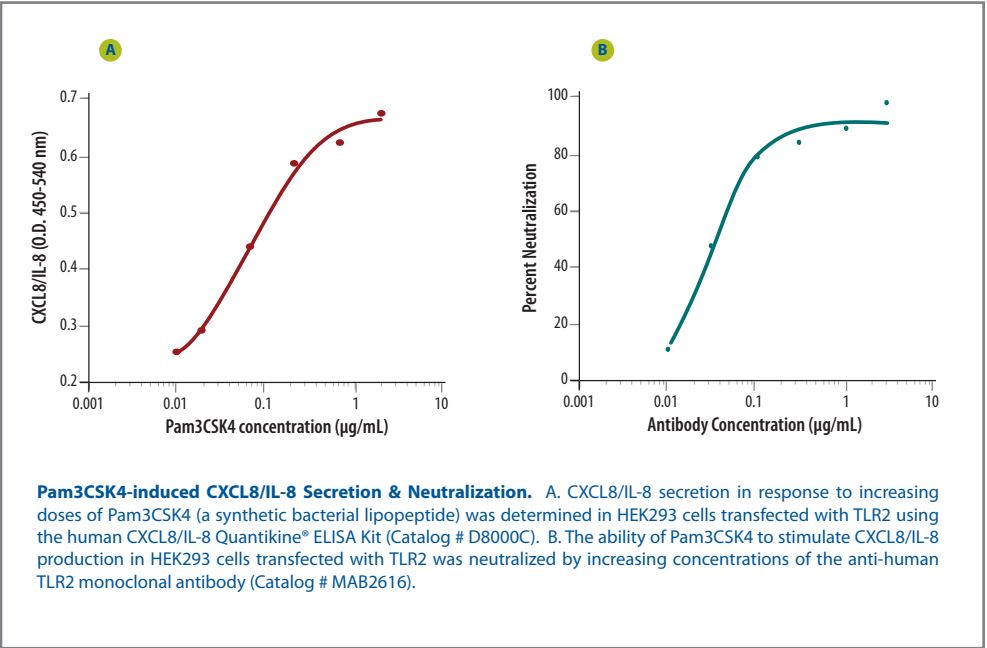
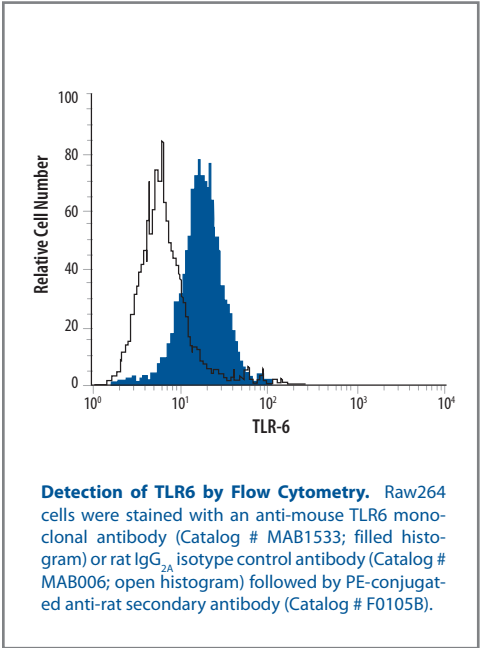


Toll-like Receptor Signaling Pathways

Toll-like receptors (TLRs) are a class of pattern recognition receptors (PRRs) in mammals that are related to the IL-1 receptor (IL-1R) superfamily. TLRs are involved in initiating the innate and adaptive immune responses following infection by microbial pathogens. They are activated upon recognition of conserved pathogen-associated molecular patterns (PAMPs) that are present in microbial proteins, nucleic acids, lipids, and carbohydrates. These PAMP-containing molecules act as ligands to trigger TLR-dependent signal transduction cascades that ultimately activate the transcription factors, AP-1, NFκB, and IRF3. AP-1 and NFκB induce the expression of pro-inflammatory cytokines (IL-1, IL-6, TNF-α), chemokines (CXCL8/IL-8, CXCL1/GROα, CCL2/MCP-1/JE, CCL3/MIP-1α, CCL4/MIP-1β,

CCL5/RANTES, CCL7/MCP-3, CCL8/MCP-2, CCL13/MCP-4), and co-stimulatory molecules. IRF3 stimulates the expression of Type I IFN-inducible genes. TLR-dependent expression of pro-inflammatory molecules at an infection site results in the recruitment of leukocytes that increase the killing of pathogenic microbes and infected cells. TLRs have a leucine-rich extracellular domain, a single transmembrane domain, and a cytoplasmic domain containing a Toll/IL-1R (TIR) motif. This domain mediates intracellular interactions between TLRs and other TIR-domain containing molecules, including adaptor proteins such as MyD88, TIRAP, TRIF, and TRAM. Humans express ten different TLRs, each recognizing a distinct set of exogenous and endogenous ligands.

Some TLRs are located on the cell surface (TLR1, 2, 4, 5, 6, 10) and specialize in the recognition of bacterial products, while others are located in intracellular compartments (TLR3, 7, 8, 9) and recognize viral nucleic acids. Different types of immune system cells each express a distinct subset of TLRs allowing vigilant surveillance for bacterial, viral, and fungal infections. Polymorphisms in the TLRs or in TLR-signaling molecules have been linked to immunodeficiencies in response to bacterial and viral infections, and to human disease conditions such as asthma, atherosclerosis, cancer, late onset Alzheimer's disease, and rheumatoid arthritis. R&D Systems offers a wide range of research reagents useful for the study of TLR signaling pathways.



TLR-Related Products

TOLL-LIKE RECEPTORS				
Molecule	Antibodies	Proteins	ELISAs/Assays	Primer Pairs
TLR1	H M	M		H M R
TLR2	H M	H M		H M R
TLR3	H M	H M		H M R
TLR4	H M	H		H M R
TLR5				H M R
TLR6	M	M		H M R
TLR9	H			H M R

TLR-SIGNALING MOLECULES				
Molecule	Antibodies	Proteins	ELISAs/Assays	Primer Pairs
c-Jun	H M			
JNK	H M R		H M R	
JNK1	H M R	H	H M R	
JNK2	H M R		H M R	
IκB-α	H			
IκB-β	H R			
IκB-ε	H M			
IKKα	H M R			
IKKβ	H			
IKKε	H M R			
IKKγ	H M R			
IRAK1	H			
IRAK4	H			
IRF3	H M			
MKK4	H			
MKK7	H			
MyD88	H M R			
NFκB1	H M			
NFκB2	H			
Phospho-JNK	H M R		H M R	
RIP1	H M R			
TAB1	H M			
TRAM/TICAM2	H M R			
TRAF-3	H M R			
TRAF-6	H			

PROTEOME PROFILER™ CYTOKINE ARRAY KITS	
Kit	Catalog #
Human Cytokine Array Kit	ARY005
Mouse Cytokine Array Kit	ARY006
Rat Cytokine Array Kit	ARY008

TLR-SIGNALING TARGETS				
Molecule	Antibodies	Proteins	ELISAs/Assays	Primer Pairs
CCL2/MCP-1/JE	H M Ca CR	H M R Ca	H M Ca	
CCL3/MIP-1α	H M CR	H M CR	H M	
CCL4/MIP-1β	H M CR	H M CR	H M	
CCL5/RANTES	H M CR	H M CR F	H M	
CCL7/MCP-3	H M	H M	H	
CCL8/MCP-2	H M	H	H	
CCL13/MCP-4	H	H	H	
CXCL1/GROα	H	H	H	
CXCL8/IL-8	H Ca F P	H Ca F P	H Ca P	H
CXCL10/IP-10	H M CR	H M CR	H M	
IFN-α	H M CR P	H M R CR F P Pr	H M	
IFN-β	H M R	H M R	H M	
IL-1α/IL-1F1	H M R CR P	H M R CR P	H M R	
IL-1β/IL-1F2	H M R Ca CR F P	H M R Ca CRE F P Pr	H M R F P	
IL-1F5/FIL1δ	H	H M		
IL-1F6/FIL1ε	H M	H M		
IL-1F7/FIL1ζ	H	H		
IL-1F8/FIL1η	H M	H M		
IL-1F9/IL-1H1	H	H		
IL-1F10/IL-1HY2	H			
IL-1ra/IL-1F3	H M E P	H M R E P	H M	
IL-6	H M R Ca CRE F P	H M R Ca CRE F P	H M R Ca F P	H M R
IL-10	H M R Ca CRE F P V	H M R Ca CRE F P V	H M R Ca F P	H M R
IL-12	H M R Ca F P	H M R Ca F P Pr	H M P	H M R
TNF-α	H M R B Ca CRE P Pr	H M R B Ca CRE F P Pr	H M R Ca E F P Pr	

TLR-ASSOCIATED MOLECULES				
Molecule	Antibodies	Proteins	ELISAs/Assays	Primer Pairs
Profilin-like Protein	Tg			
RP105	M			H

Abbreviation Key: **B**: Bovine **Ca**: Canine **CR**: Cotton Rat **E**: Equine **F**: Feline **H**: Human **M**: Mouse **P**: Porcine **Pr**: Primate **R**: Rat **Tg**: *T. gondii* **V**: Viral